REMARKS

Claims 8 and 41 are cancelled by this amendment. Claims 1-6, 9-31, 33-40, and 42-56 will be pending after the entry of this amendment. Claims 1 and 5 have been amended. The amendments are supported at least by the disclosures in page 13, lines 24-33; page 41, line 30 to page 42, line 7; and claim 1. Claims 42-45 have been amended to replace "allogeanic" with "allogenic" to correct a spelling error. Claims 49-52 have been amended to depend on claim 1.

Objections to Claims 8 and 33

Applicants respectfully traverse the objections to claims 8 and 33 in page 2 of the Office Action.

Claim 8 has been cancelled, rendering the objection to this claim moot. Claim 33 is directed to a production **method** of a G0 transgenic chimera bird. It is an essential feature of the claimed **method** to use VSV-G pseudo type to achieve high infectivity. *See* page 10, lines 21-23; page 15, lines 13-18 of the specification. Thus, Applicants respectfully request the withdrawal of the objection to claim 33.

Claim Rejections Under 35 USC 112

Applicants respectfully traverse the rejections of claims 1-6 and 8-25 under 35 USC 112, the second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

The phrase "introduced therein" in claim 1 has been deleted. The phrase "a transgene" in claim 1 has been replaced with "the exogenous antibody gene."

With respect to the phrase "derived from" in claims 1 and 25, the Office Action states in page 4 that "[n]either the claims nor the specification disclose what retroviral vector portion derived from a MoMLV vector is the essential feature of the invention." However, the specification discloses "5'LTR and 3'LTR each represents a long terminal repeat sequence of MoMLV" (page 12, lines 16-17; page 13, lines 32-33; page 14, lines 4-6). This disclosure is sufficiently definite to make clear the "metes and bounds" of the term "derived from." Thus, claims 1 and 25, sufficiently supported by the disclosure in the specification, do not fail to "particularly point out and distinctly claim the subject matter which the Applicant regards as his

invention." Applicants respectfully request the withdrawal of the rejections to claims 1-25 under 35 USC 112.

The phrase "the antibody gene" in claim 5 has been replaced with "either or both of the light chain gene or the heavy chain gene of the antibody" to make it clear that either or both of the light chain gene or the heavy chain gene of the antibody is to be controlled by the constitutive promoter recited in claim 5. The amendment is supported at least by the disclosure in page 13, lines 24-33 and page 41, line 30 to page 42, line 7.

In claims 42-45, "allogeanic" has been replaced with "allogenic."

By these amendment, Applicants submit that the claims 1-6 and 8-25 now fully compliant with 35 USC 112, the second paragraph.

Claim Rejections Under 35 USC 102

Applicants respectfully traverse the rejections of claims 1, 5, 8-9, 24, and 41-56 as being anticipated by Ivarie et al. (US 6,730,822), the rejections of claims 1, 5, 8-16, 24, 41, and 44-56 as being anticipated by Rapp et al. (US 2002/0108132), and the rejections of claims 1-5, 8-16, 24, and 41-56 as being anticipated by Rapp et al. (US 2003/0126629), as evidenced by Kines et al (Exp. Parasitol. 112(4): 209-220, 2006; Abstract only).

The Office Action states in page 10 that the transgenic bird in the present claims is structurally indistinguishable from the birds in the cited references. This statement, however, is incorrect. None of the cited references, Ivarie et al. (US 6,730,822), Rapp et al. (US 2002/0108132), and Rapp et al. (US 2003/0126629), **actually** discloses the production of transgenic birds with exogenous antibody genes. In addition, the present invention overcomes the silencing mechanism by infecting a virus vector at the specific time frame (Example 5, page 30, lines 9-24). One of the essential features of the present invention is that virus infection is carried out after and exclusive of a blastodermal period, which enables one to achieve **efficient expression** of exogenous transgene (page 11, lines 8-13; claim 25; Example 5, page 30, lines 9-23; Figures 2 and 3). This feature is not disclosed in any of the references. Furthermore, the transgene expression in the present application is **more efficient** than that in the references. Ivarie et al. (US 6,730,822) discloses that β-lactamase was expressed at 20-40 mg/egg (column 23, line 16), or ~1 mg/ml "assuming 40 mls of egg white per egg" (column 23, line 1), in the eggs of G1 bird and that lower expression was observed in the eggs of G0 bird (column 22, line

66 to column 23, line 1). Rapp et al. (US 2003/0126629) discloses that β-lactamase and interferon was expressed at 0.0325 mg/ml and ~0.007 mg/ml in eggs, respectively (paragraphs [0337], [0364], Fig. 16, and Fig. 17). The amount of transgene expression in eggs is not disclosed in the other references. Compared to the amount of expression in Ivarie et al. (US 6,730,822), and Rapp et al. (US 2003/0126629), the sum of scFv-Fc antibody expressed in total egg of G0 bird in the present application is approximately 2 mg/ml (Fig. 15), more than twice of the amount of transgene expression in Ivarie et al. (US 6,730,822) and more than six times of that amount in Rapp et al. (US 2003/0126629). The fact that the amount of transgene expression in the eggs of G0 birds is far more than the amount disclosed in the references is at least some evidence that the transgenic birds in the product-by-process claims 1-23, and its dependent claim 24, are **structurally distinct** from those in the cited references.

U.S. application No. 10/585693 (US 2007/0214511), an application by the same applicant, discloses that G2 birds (descendants of the G0 bird in the present invention) produces comparable transgene expression with G0 birds (Table 4 in paragraph [0136]), demonstrating that the efficient expression in G0 bird is **inherited** to their descendents. Therefore, claims 42-48 and 53-56, which recite G1 and G2 birds, are not anticipated by the cited references either.

Claims 49-52 have been amended to depend on claim 1. In amended claims 49-52, the exogenous transgene is limited to an antibody gene. These amended claims are not anticipated by the cited references because none of the references, as discussed above, **actually** discloses the production of a transgenic bird expressing an antibody gene.

For at least the foregoing reasons, Applicants respectfully request the withdrawal of the claim rejections under 35 USC 102.

Rejections to Claims 1-24 Under 35 USC 103(a)

Applicants respectfully traverse the rejections under 35 USC 103(a) of claims 1, 5, 8-16, 24 and 41-59 as being unpatentable over Ivarie et al. (US 6,730,822) and Rapp et al. (US 2002/0108132); the rejections of claims 1-4 as being unpatentable over Ivarie et al. (US 6,730,822) and Rapp et al. (US 2002/0108132), as applied to claims 1,5, 7-16, 24 and 41-59 above, and in further view of Chad et al. (Curr. Op. Biotechnology 12(2):188-194; 2001); the rejections of claims 1 and 6 as being unpatentable over Ivarie et al. (US 6,730,822), Rapp et al. (US 2002/0108132), and Chad et al. (Curr. Op. Biotechnology 12(2):188-194; 2001), as applied

to claims 1-5, 7-6, 24 and 41-59 above, and in further view of Guild et al. (J. Virology 62(10):3795-3801; 1988); and the rejections of claims 1 and 17-23 as being unpatentable over Ivarie et al. (US 6,730,822), Rapp et al. (US 2002/0108132), Chad et al. (Curr. Op. Biotechnology 12(2):188-194 and ; 2001) and Guild et al. (J. Virology 62(10):3795-3801; 1988), as applied to claims 1-16, 24 and 41-59 above, and in further view of Powers et al. (J. Immunol. Methods 251:123-135; 2001), as evidenced by Ono et al (J. Biosci. And Bioeng. 95(3): 231-238, 2003).

The Office Action states in page 15 that the transgenic bird in the present claims is structurally indistinguishable from the birds in the cited references. However, as discussed above, the amount of transgene expression in the eggs of G0 birds is far more than the amount disclosed in the references. It is evident that the transgenic birds in the present application are **structurally distinct** from those in the cited references.

As discussed above, the eggs of the G2 bird show comparable transgene expression with the G0 birds of the present invention (Table 4 in paragraph [0136] in U.S. application No. 10/585693 (US 2007/0214511)), demonstrating that the escape from silencing mechanism is **inherited** to the claimed descendants.

The Office Action states that the degree or mechanism of transgene silencing is not germane because the cited references disclose transgenic birds achieving the instantly claimed yields of heterogeneous protein when harvested from the instantly claimed tissues. Out of the cited references, only Ivarie et al. (US 6,730,822) and Rapp et al. (US 2003/0126629) disclose the amount of transgene expression in transgenic bird, which is less than half of the amount of transgene expression in the present application. Moreover, the transgenes used in Ivarie et al. (US 6,730,822) (β-lactamase (column 23, line 16)) and Rapp et al. (US 2003/0126629) (β-lactamase and interferon (paragraphs [0337], [0364], Fig. 16, and Fig. 17)), are different from the transgene (an exogenous antibody gene, claim 1) in the present invention. It is well known to one skilled in the art that the amount of gene expression varies according to the gene used. It is incorrect to conclude that that the degree or mechanism of transgene silencing is not germane by simply comparing the amount of transgene expression in the references that use different transgenes from the instant application with the amount of transgene expression in the instant application.

For at least the above reasons, Applicants respectfully request the withdrawal of the rejections of claims 1-24 under 35 USC 103(a).

Rejections to Claims 25-56 Under 35 USC 103(a)

In the pending Office Action, paragraphs 6 and 10-14 apply various combinations of Mizuarai et al. (J. Biochem. 129:125-132; Jan. 2001), Ivarie et al. (U.S. Patent No. 6,730,822), Schatten et al. (Publication No. 2003/0221206); Guild et al. (J. Virology 62(10):3795-3801; 1988); Rapp et al. (Publication No. 2002/0108132); and Powers et al. (J. Immunol. Methods 251:123-135; 2001) in a rejection under 35 USC 103 against claims 25-56. Applicants respectfully traverse these rejections.

Although Mizuarai discloses infecting an early embryo, e.g. "a 48-hour stage [quail] embryo" (Mizuarai et al., page 127, col. 2, lines 1-5) within the cited time frame, Mizuarai intends to show that higher infectivity is achieved when the virus infection is performed with the protamine-modified lipid vesicles, compared to the infection with virus vectors only (page 129, the bridging paragraph between col. 1 and col. 2; page 130, Fig.6). An essential feature of the present invention is the **enhanced transgene expression** imparted by infecting an early embryo after and exclusive of a blastodermal period (page 11, lines 8-13; Example 5, page 30, lines 9-23; Figures 2 and 3; claim 25). Mizuarai does not recognize or suggest the unexpected effect of **enhancing transgene expression** imparted by infecting an early embryo. Without a recognition of this unexpected effect, there is no reason to modify any of the above references to infect the embryo after and exclusive of a blastodermal period immediately after the spawning with a replication-defective retrovirus vector.

For at least the foregoing reasons, claims 25-56 are patentable over the references applied in paragraphs 6 and 10-14 of the pending Office Action. Applicants respectfully request the withdrawal of the rejections of claims 25-56 under 35 USC 103(a).

Double Patenting

In the pending Office Action at paragraphs 15-16, the specified claims are provisionally rejected on the ground of non-statutory obviousness type double patenting over claims 6-14 and 17-22 of copending Application No. 10/569,268 and over claims 1-30 of copending Application

No. 10/585,693. As these rejections are provisional, Applicants respectfully request that these rejections be held in abeyance until these are the only remaining rejections in this application.

CONCLUSION

It is respectfully submitted that the present application is now in condition for allowance, which action is respectfully requested. The Examiner is invited to contact Applicants' representative to discuss any issue that would expedite allowance of the subject application.

Any fees for extension(s) of time or additional fees are required in connection with the filing of this response, such extensions of time are hereby petitioned under 37 C.F.R. § 1.136(a), and the Commissioner is authorized to charge any such required fees or to credit any overpayment to Kenyon & Kenyon's Deposit Account No. 11-0600.

Respectfully submitted,

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